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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/071,822	02/08/2002	Gregory E. Hardee	ISIS-4947	4141

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EXAMINER	
GIBBS, TERRA C	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 01/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/071,822	HARDEE ET AL.	
	Examiner	Art Unit	
	Terra C. Gibbs	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26,27,29 and 30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26,27,29 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 6, 2005 has been entered.

Claims 26 and 27 have amended. New claims 29 and 30 are acknowledged.

Claims 26, 27, 29, and 30 are pending in the instant application.

Claims 26, 27, 29, and 30 have been examined on the merits.

Response to Amendment

Applicants Amendment filed December 6, 2005 has been considered. Rejections and/or objections not reiterated from the previous office action mailed September 7, 2005 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 26 and 27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 26 introduces new matter into the disclosure because it recites the limitation, "wherein said carrier particles have a diameter of about 0.1 to about 1000 microns". The response filed December 6, 2005 indicates that support for this limitation can be found at the end of paragraph [0010]. It is noted that the end of paragraph [0010] recites, "carrier particles have a diameter of about 0.01 to 1000μ". While Applicants have support for carrier particles that have a diameter of about 0.01 to 1000μ, the range of 0.01 to 1000μ does not support the specific range of 0.1 to 1000μ as instantly claimed. Therefore the limitation "wherein said carrier particles have a diameter of about 0.1 to about 1000 microns" is new matter.

Therefore, claim 26 and claim 27 that depends therein contains new matter.

Applicant is required to cancel the new matter in the reply to this Office Action.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 26-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 26 appears to contain a typographical error since it has a dash in between the words "delivering" and "an" in line 1.

Therefore, claim 26 and claims that depend therein are indefinite. Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 26, 27, 29, and 30 are rejected under 35 U.S.C. 102(a) as being anticipated by Dean et al. [WO 98/49348].

Claim 26 is drawn to a method of delivering an oligonucleotide across a mucosal membrane in a human, comprising a plurality of carrier particles, an oligonucleotide, and capric acid, wherein said carrier particles have a diameter of about 0.1 to about 1000 microns. Claims 27, 29, and 30 are dependent on claim 26 and include all the

limitations of claim 26, with the further limitations, wherein said plurality of carrier particles is administered orally, wherein said carrier particles have a diameter of about 0.1 to about 500 microns; and wherein said carrier particles have a diameter of about 1 to about 300 microns.

It is noted that the instant specification at page 3, paragraph [0010] discloses, "carrier particles according to the present invention include a variety of particle-forming substances". The instant specification at page 3, paragraph [0010] also discloses, "preferred carrier particles are those which enhance bioavailability of a biologically active substance upon administration and delivery to a mucosal membrane". Dean et al. disclose at Table 1, compound 2302, when administered with water or saline, exhibited 1-2% plasma bioavailability. Dean et al. also disclose at Table 1, compound 2302, when administered with bile salt (2% CDCA) alone exhibited 11% bioavailability. However, compound 2302, when administered with bile salt plus fatty acids (4% Na caprate, Na laurate), exhibited 14.6% bioavailability (see Table 1). In this regard, the bile salt and fatty acids disclosed in Table 1 each individually enhanced bioavailability of an active substance upon administration and delivery to a mucosal membrane. Therefore, the bile salt and the fatty acid administered with compound 2302 in Table 1 both independently represent a "plurality of carrier particles" and thus anticipate the instant claims.

It is noted that the Dean reference is silent regarding the specific size(s) of the carrier particles used in their method of delivering an oligonucleotide across a mucosal membrane. However, since the Patent Office cannot determine the actual sizes of the

carrier particles of the prior art, the burden of establishing whether the prior art carrier particles are within the size limitations recited in the instant claims falls to Applicant. See MPEP 2112.01, "Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. In re Best, 562 F.2d at 1255, 195 USPQ at 433." See also MPEP 2112: "[T]he PTO can require an Applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [her] claimed product." The MPEP at 2112 citing *In re Fitzgerald* 205 USPQ 594. 596, (CCPA 1980), quoting In re Best 195 USPQ 430 as per above. Therefore, it falls to Applicant to determine and provide evidence that the prior art carrier particles would or would not fall within the size limitations as recited in the instant claims.

Therefore, absent evidence to the contrary, Dean et al. anticipate the instant claims.

Response to Arguments

It is noted that in the previous Office Action mailed September 7, 2005, the same rejection was maintained.

In response to this rejection, Applicants argue that Dean et al. provides no teachings or suggestions regarding carrier particles of specific sizes as now claimed.

Applicant's arguments have been fully considered, but are not found persuasive. The Examiner agrees that the Dean reference is silent regarding the specific size(s) of the carrier particles used in their method of delivering an oligonucleotide across a mucosal membrane. However, it falls to Applicant to determine and provide evidence that the prior art carrier particles would or would not fall within the size limitations as recited in the instant claims. See MPEP 2112.01 and discussion above.

Further, the claims are so broad to include a diameter as low as *about* 0.1 microns (100 nanometers) to as high as *about* 1000 microns ($1x10^6$ nanometers). Given the fact that the carrier particles disclosed by Dean et al. traverse the mucosal membrane, they clearly have to be within the size range of *about* 0.1 to *about* 1000 microns as instantly claimed, absent evidence to the contrary. Further, the term "about" is considered to be open language and can include a very broad range of diameter sizes. For example, 5,000 microns can be interpreted to be *about* 1,000 microns. Applicants are directed to MPEP 2173.05(b) which states:

> "About"
> The term "about" used to define the area of the lower end of a mold as between 25 to about 45% of the mold entrance was held to be clear, but flexible. Ex parte Eastwood, 163 USPQ 316 (Bd. App. 1968). Similarly, in W.L. Gore & Associates, Inc. v. Garlock, Inc., 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), the court held that a limitation defining the stretch rate of a plastic as "exceeding about 10% per second" is

definite because infringement could clearly be assessed through the use of a stopwatch.

In summary, Dean et al. do not disclose the diameter of the specific size(s) of the carrier particles used in their method of delivering an oligonucleotide across a mucosal membrane. However, it falls to Applicant to determine and provide evidence that the prior art carrier particles would or would not fall within the size limitations as recited in the instant claims. Further, the carrier particles clearly permeate the membrane and therefore must be within the size range as recited in the instant claims, absent evidence to the contrary. The term "about" is considered to be open language and since the claims are so broad to recite "about 0.1 to about 300 microns", for example, the Examiner is of the opinion that the carrier particles used in the method disclosed by Dean et al. are about 0.1 microns (100 nanometers) to about 300 microns ($3x10^5$ nanometers) as instantly claimed, since they traversed the mucosal membrane.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is 571-272-0758. The examiner can normally be reached on 9 am - 5 pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

tcg
January 19, 2006

SEAN McGARRY
PRIMARY EXAMINER
1635